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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,942	06/21/2001	Juha Punnonen	0179.210US	4876

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MAXYGEN, INC.
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EXAMINER

LEFFERS JR., GERALD G

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 07/30/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/886,942

Applicant(s)

PUNNONEN, ET AL

Examiner

Gerald G Leffers Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 7, 8, 10-12, 14-18, 21-24, 26-28, 30-36, 44-48, 62-66, 74-79, 93, 94 and 105-119 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other _____

Continuation Sheet (PTO-326)

Application No. 09/886,942

Continuation of Disposition of Claims: Claims pending in the application are 1-4, 7, 8, 10-12, 14-18, 21-24, 26-28, 30-36, 44-48, 62-66, 74-79, 93, 94 and 105-119.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 5/9/03 as Paper No. 19, in which several claims were amended (claims 1-4, 7-8, 10, 12, 14, 17-18, 21-24, 26-28, 30-36, 46, 62, 65, 93-94, 105-107), several claims were cancelled (claims 13, 19-20, 25, 29, 37-43, 104) and in which new claims were added (claims 108-119). Claims 1-4, 7-8, 10-12, 14-18, 21-24, 26-28, 30-36, 44-48, 62-66, 74-79, 93-94, 105-119 are pending and under consideration in the instant application.

Any rejection of record in the previous office action (Paper No. 16 mailed 12/6/02) that is not addressed herein is withdrawn. This action is not final due to new grounds of rejection made herein that were not necessitated by applicant's amendment of the claims in Paper No. 19.

Information Disclosure Statement

The information disclosure statement filed 1/24/03 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the copies of the cited references are not in the file. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. The examiner acknowledges that applicant provided evidence that the first set of references filed with the IDS filed 12/13/01 was received by the Office. However, none of the references submitted either time have been matched with the file. The examiner can obtain copies of the U.S. Patents and international applications cited on the submitted PTO 1449 forms. It is respectfully requested that applicant submit a hand-carried copy of the other publications listed on the PTO 1449 forms to the Office to insure that the examiner can review each of the references. No fees would be due upon such a delivery.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-11, 21-24, 26-28, 30-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicant's amendment of the claims in Paper No. 19.**

Each of these claims comprises a limitation wherein the claimed nucleic acid comprises a sequence of, or difference in sequence with, SEQ ID NO: 8 as it corresponds to the consensus sequence in Figures 8A-8I. There is no literal or inherent support anywhere in the specification as filed for claiming the nucleic acid of the invention as they related to SEQ ID NO: 8 in comparison to the consensus sequence in Figures 8A-8I. Therefore, these newly added limitations are impermissible new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 7-8, 12, 14-18, 21-24, 26-28, 30-36, 44-48, 62-66, 74-79, 93-94, 105-119 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly

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point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections.**

Claims 1, 7, 8, 106 comprise the limitation of “at least about 98% [or 99%] sequence identity”. The specification doesn’t teach exactly what is meant by the term “at least about” when applied to percent sequence identity. Does the term necessarily mean a range of +/- 5%? Or +/- 1%? Or +/- .5%? The description provided in the instant application indicates a series of preferred percent identities for the nucleic acids of the invention ranging from 70% to 99.5%, yet there is consistent interval between the different percentages and no explicit definition for the term “at least about” so that the skilled artisan is unable to assume what nucleic acids will necessarily be encompassed by the rejected claims.

Claims 17-18 are vague and indefinite in that the metes and bounds of the phrase “higher than the highest expression level” of the polypeptide-encoding sequence are unclear. The phrase “higher than the highest level” is inherently indefinite in that absence of specific definition of the host cell or *in vitro* conditions in which the “highest level” of expression is determined. Expression of a heterologous coding sequence from the claimed polynucleotide sequence will vary from cell to cell, condition to condition, making it impossible for the skilled artisan to know whether the levels observed in a particular system are the “highest level” or not.

Claim 74 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term “the subset” in part (b) of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

Claims 1-3, 7-8, 12, 14-18, 21-24, 26-28, 30-36, 44-48, 63-66, 74-78, 104-105, 107-119 are rejected under 35 U.S.C. 102(b) as being anticipated by Chapman et al (Nucleic Acids Research, 1991, Vol. 19, No. 14, pages 3979-3986; see the entire document). **This rejection is maintained for reasons of record in Paper No. 16, mailed 12/6/02 and repeated below. These grounds of rejection are extended to claims 63-66 and new claims 108-119.**

Chapman et al teach the construction and characterization of expression constructs comprising variations of a 2.4 kb fragment obtained for the hCMV Towne strain. The 2.4 kb hCMV sequence characterized by Chapman et al comprises total identity to SEQ ID NO: 8 of 95.8% and a local similarity of 98.8% over residues 335-2099 of the 2.4 kb sequence (e.g. see the attached search report, pages 11-12, result 9). The fragments characterized by Chapman et al were demonstrated as driving expression of different coding sequences used as reporters for promoter activity (e.g. Tables I and II).

Various of the rejected claims comprise limitations where the claimed nucleic acid drives expression of a reporter sequence at different levels relative to expression of the same reporter from a given reference CMV promoter. Given the levels of expression for the different constructs characterized by Chapman et al, and given the high degree of identity to the constructs taught in the instant application, one of skill in the art would recognize that the constructs taught

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by Chapman et al would necessarily comprise the recited characteristics concerning expression levels in comparison to the reference CMV promoter. Similarly, one of skill in the art would recognize that the constructs of Chapman et al would express the encoding sequences well enough to induce an immune response in at least expression system.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 1-3, 7-8, 12, 14-18, 21-24, 26-28, 30-36, 44-48, 63-66, 74-78, 104-105, 107-119 are rejected under 35 U.S.C. 102(b) as being anticipated by Bebbington (WO 89/01036 A1; see the entire published application) or (WO 89/01036 A2; see the entire published application).

This rejection is maintained for reasons of record in Paper No. 16, mailed 12/6/02 and repeated below. These grounds of rejection are extended to claims 63-66 and new claims 108-119.

Bebbington teaches the construction and use of expression vectors comprising the complete 5'-untranslated region including the first intron of the major immediate early gene of human cytomegalovirus (e.g. the Abstract). The sequences taught by Bebbington comprise ~95.9% sequence identity to SEQ ID NO: 8. Local similarity over ~1.77kb of the Bebbington

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promoter sequence reaches levels of up to 97.8% identity with the entire sequence of SEQ ID NO: 8 (e.g. see pages 1-3 of the attached search report for SEQ ID NO: 8).

Various of the rejected claims comprise limitations where the claimed nucleic acid drives expression of a reporter sequence at different levels relative to expression of the same reporter from a given reference CMV promoter. Given the levels of expression for the different constructs characterized by Bebbington, and given the high degree of identity to the constructs taught in the instant application, one of skill in the art would recognize that the constructs taught by Bebbington would necessarily comprise the recited characteristics concerning expression levels in comparison to the reference CMV promoter. Similarly, one of skill in the art would recognize that the constructs of Bebbington would express the encoding sequences well enough to induce an immune response in at least one expression system.

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Response to Arguments

Applicant's arguments filed in Paper No. 19 with regard to prior art rejections of record have been fully considered but they are not persuasive. In Paper No. 19, the response essentially argues the following: 1) the teachings of Chapman et al and Bebbington are not applicable to the amended claims as neither reference teaches a nucleic acid with "at least about" 98% or 99%

identity to SEQ ID NO: 8, 2) the examiner has chosen an arbitrary subsequence of Chapman et al for comparison to SEQ ID NO: 8, 3) Chapman explicitly *teaches away* from the claimed invention, 4) none of the fragments taught by Chapman et al meet the identity limitations recited in the amended claims, 5) the facts of In re Best do not apply here, 6) the sequences taught by Bebbington do not satisfy the percent identity requirements of the amended claims, 7) Bebbington does not teach or suggest that any specific fragment of their sequence will function to drive transcription, 8) the sequences taught by Bebbington differ dramatically in structure from those claimed.

With regard to the assertion that the examiner has chosen arbitrary sequences that are not taught specifically by the cited references as meeting the functional limitations of the claims, the claims actually encompass the larger fragments that were used to generate the percent identities cited in making the rejection, for the following reasons. As indicated in the specification, percent identity can be determined by a number of different algorithms using different parameters, over which the degree of “identity” for two given sequences will vary. While the instant specification does provide some guidance as to the basic parameters for different sequence comparison algorithms (e.g. BLAST N), no specific parameters are recited in the claims. Thus, newly added claims reciting “at least” 99% or 99.5% identity have been included in the rejections of record. Moreover, the instant specification does not provide a specific definition for the term “at least about” as applied to percent identity between two nucleic acid sequences (see above). Therefore, the recited claim limitations of “at least about” 98% or 99% identity with SEQ ID NO: 8 encompass the sequences taught by Chapman et al and Bebbington.

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Because these sequences are still embraced by the rejected claims, it is hard to see how they differ structurally from those claimed.

With regard to so called teachings away by Chapman or Bebbington, the issue of "teaching away" is not one that normally is relevant for rejections made for anticipation under 35 U.S.C. 102. However, the examiner has made rejections based upon an argument of inherency and the arguments concerning "teaching away" are somewhat relevant in determining if the limitations at issue "necessarily flow" from the cited references. The examiner contends, at least with regard to the larger sequences used to make the sequence identity comparison, that the teachings of Chapman et al and Bebbington make clear the sequences have promoter activities.

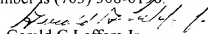
Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
July 28, 2003